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DT04 Rec'd PCT/PTO 29 JUN 2004  
PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Jean-Erick ANCEL Attn: PCT Branch

Application No. New U.S. National Stage of PCT/EP03/00231

Filed: June 29, 2004 Docket No.: 120132

For: PROCESS FOR THE PREPARATION OF PHYTONE

**SUBMISSION OF THE ANNEXES TO THE  
INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Attached hereto is a submission of the annexes to the International Preliminary Examination Report (Form PCT/IPEA/409). The attached material replaces the claims.

Respectfully submitted,



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Date: June 29, 2004

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**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**  
 (PCT Article 36 and Rule 70)

Rec'd PCT/PTO 29 JUN 2004

Applicant's or agent's file reference A84B45674 MD	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP03/00231	International filing date (day/month/year) 13.01.2003	Priority date (day/month/year) 14.01.2002
International Patent Classification (IPC) or both national classification and IPC C07C45/69		
Applicant ADISSEO FRANCE S.A.S. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I  Basis of the opinion
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 26.05.2003	Date of completion of this report 31.10.2003
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Pérez Carlon, R  Telephone No. +49 89 2399-8125



INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

International application No.

PCT/EP03/00231

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-6 as originally filed

**Claims, Numbers**

1-12 received on 09.10.2003 with letter of 09.10.2003

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/EP03/00231**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-12
	No: Claims	
Inventive step (IS)	Yes: Claims	1-12
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-12
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP03/00231

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or  
industrial applicability; citations and explanations supporting such statement**

D1: EP-A-0 737 663

D2: EP-A-0 816 321

1. The present application claims an intermediate (I) in the synthesis of phytone (claim 7) a process for obtaining it (claim 1) and a process for the preparation of phytone by using said intermediate (claim 8)

Intermediate (I) is obtained by coupling an acetylenic compound (III) and a terminal olefin (II) in a total synthetic strategy  $C_8 + C_{10} \rightarrow C_{18}$  (I)  $\rightarrow$  phytone

- 2.1 Document D1 describes the coupling of acetylenic compounds and  $\alpha,\beta$ -unsaturated ketones. None of the starting materials (III) and (II) as in the application are disclosed.
- 2.2 Document D2 describes a synthesis of phytone through a totally different process (see scheme on p. 3) that implies  $C_8 \rightarrow C_{12} \rightarrow C_{18} \rightarrow$  phytone.

Claims 1-12 are new in the sense of Art. 33(2) PCT.

3. In light of the state of the art, the problem to be solved can be regarded as to the provision of an alternative synthesis of phytone.
4. The problem is solved by the process of claim 1, leading to the intermediate (I) (claim 7) that is further (claim 8) hydrolysed and hydrogenated to allow the obtention of the phytone.
5. No indications were found that could have led the skilled man to choose this particular strategy in order to solve the problem posed. It also has to be noted that D1 refers to the coupling of conjugated olefines, whereas the terminal olefin (II) as in the application is not conjugated. The synthesis of D2 uses a completely different strategy, from which the present approximation cannot be deduced.

Claims 1-12 are regarded as inventive, in the sense of Art. 33(3) PCT.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP03/00231

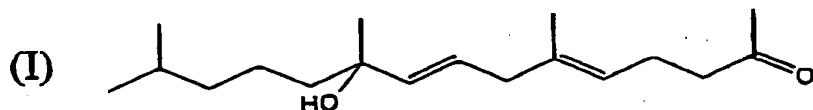
6. There are no doubts about industrial applicability (Art. 33(4) PCT).

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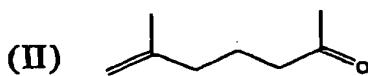
## CLAIMS

1. Accordingly, the present invention provides a process for the preparation of a compound of formula (I)

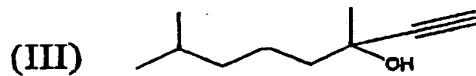


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which comprises reacting a compound of formula (II)



with a compound of formula (III)



10 in the presence of a catalyst and a polar solvent.

2. A process as claimed in claim 1 in which the polar solvent is selected from dimethylformamide, dimethylacetamide, dimethylsulfoxide or N-methyl pyrrolidone

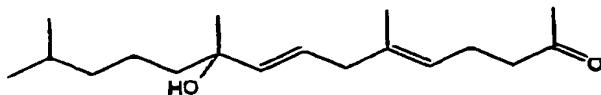
15 3. A process as claimed in claim 1 or claim 2 in which the catalyst is selected from cationic divalent ruthenium complexes such as cyclopentadienyl ruthenium hexafluorophosphate tris - acetonitrile, or pentamethyl-cyclopentadienyl ruthenium hexafluorophosphate tris - acetonitrile

20 4. A process as claimed in any one of the preceding claims carried out in the presence of a second solvent, said second solvent being immiscible with the first solvent.

25 5. A process as claimed in claim 4 in which the second solvent is an apolar solvent selected from aliphatic or aromatic hydrocarbons.

6. A process as claimed in any one of the preceding claims carried out at a temperature of from 20 to 100°C and under atmospheric pressure.

7. Novel compound characterised by the following structure

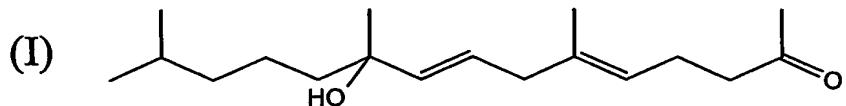


8. A process for the preparation of phytone which comprises (a) a first step of hydrolysing the compound as claimed in claim 7 to produce a hydrolysis product; and (b) a second step of hydrogenating the hydrolysis product of step (a)
- 5 9. A process as claimed in claim 8 wherein the first step is carried out in the presence of an acid catalyst selected from sulphonic acid, sulphuric acid and hydrogen chloride.
- 10 10. A process as claimed in any one of claim 8 or claim 9 in which the first step is carried out in the presence of an organic solvent selected from an organic hydrocarbon and an ether.
- 15 11. A process as claimed in any one of claims 8 to 10 in which the second step is carried out in the presence of hydrogen and a metal or metal salt selected from palladium or platinum, Raney nickel optionally in the presence of iron, manganese, cobalt, copper, zinc or chromium; zinc in the presence of acetic acid; stannous chloride; and molybdenum (III) salts.
12. A process as claimed in claim 11 wherein the catalyst is palladium supported on charcoal.

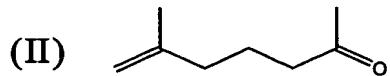
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CLAIMS

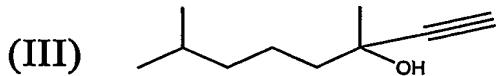
1. Accordingly, the present invention provides a process for the preparation of a compound of formula (I)



which comprises reacting a compound of formula (II)

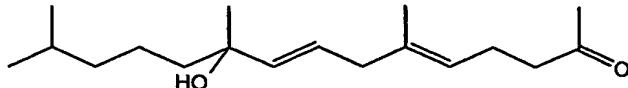


with a compound of formula (III)



in the presence of a catalyst and a polar solvent.

2. A process as claimed in claim 1 in which the polar solvent is selected from dimethylformamide, dimethylacetamide, dimethylsulfoxide or N-methyl pyrrolidone
3. A process as claimed in claim 1 or claim 2 in which the catalyst is selected from cationic divalent ruthenium complexes such as cyclopentadienyl ruthenium hexafluorophosphate tris – acetonitrile, or pentamethyl-cyclopentadienyl ruthenium hexafluorophosphate tris – acetonitrile
4. A process as claimed in any one of the preceding claims carried out in the presence of a second solvent, said second solvent being immiscible with the first solvent.
5. A process as claimed in claim 4 in which the second solvent is an apolar solvent selected from aliphatic or aromatic hydrocarbons.
6. A process as claimed in any one of the preceding claims carried out at a temperature of from 20 to 100°C and under atmospheric pressure.
7. Novel compound characterised by the following structure



8. A process for the preparation of phytone which comprises (a) a first step of hydrolysing the compound as claimed in claim 6 to produce a hydrolysis product; and (b) a second step of hydrogenating the hydrolysis product of step (a)
9. A process as claimed in claim 8 wherein the first step is carried out in the presence of an acid catalyst selected from sulphonic acid, sulphuric acid and hydrogen chloride.
10. A process as claimed in any one of claim 8 or claim 9 in which the first step is carried out in the presence of an organic solvent selected from an organic hydrocarbon and an ether.
11. A process as claimed in any one of claims 8 to 10 in which the second step is carried out in the presence of hydrogen and a metal or metal salt selected from palladium or platinum, Raney nickel optionally in the presence of iron, manganese, cobalt, copper, zinc or chromium; zinc in the presence of acetic acid; stannous chloride; and molybdenum (III) salts.
12. A process as claimed in claim 11 wherein the catalyst is palladium supported on charcoal.
13. Vitamin E obtained from a phytone characterised in that the phytone is prepared by a process according to any one of claims 8 to 12.